## REMARKS

Applicants thank the Examiner for the courtesies extended in the interview held on May 3, 2007. Claims 25-30, 50 and 57 are pending. Claim 25, 50 and 57 are amended.

Claim 25 is amended to further clarify that SEQ ID NO:12 is used for numbering, and is not required to be the only parent. In particular, the claims recite that the positions correspond to the recited in positions in SEQ ID NO:12. Claims 25, 30 and 57 have also been amended to recite that the amino acid sequence is "shown in" SEQ ID NO:12.

It is respectfully submitted that the present amendment and response places this case in condition for allowance. No new matter or new issues have been presented. Reconsideration of the application in view of the following remarks is respectfully requested.

### I. The Rejection of Claims 25-30, 50 and 57 under 35 U.S.C. 112

Claims 25-30, 50 and 57 are rejected under 35 U.S.C. 112, as allegedly lacking enablement. This rejection is respectfully traversed.

To satisfy the enablement requirement, the scope of the claims must bear a reasonable relationship to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970). "To be enabling...a patent must contain a description that enables one skilled in the art to make and uses the claimed invention." *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991). "That some experimentation is necessary does not constitute a lack of enablement; the amount of experimentation, however, must not be unduly extensive." Id.

Applicants respectfully submit that the specification enables the claimed invention commensurate in scope of the claims. The claims are directed to variant alpha-amylases having a very high degree of amino acid sequence homology to SEQ ID NO:12, namely at least 90%. The claims also encompass only functional variant alpha-amylases as the claims require that the variant has alpha-amylase activity. Although the claims refer to sequences that have 90% homology to SEQ ID NO:12, the claims also require that such sequences have a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering). As such, the claims encompass a specific subset of polypeptides having at 90% homology and having a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458.

Based on the high degree of amino acid sequence homology recited in the claims, the polypeptides falling within the scope of the claims are reasonably expected to have a very high degree of both structural and functional similarity to the reference sequence, SEQ ID NO:12. An

artisan is able to practice the claimed invention commensurate in scope with the claims as an artisan is routinely able to obtain highly homologous sequences related to SEQ ID NO:12 using well-known molecular biological techniques. Requiring at least 90% homology with SEQ ID NO:12 makes the variants sufficiently similar in terms of structure and function so that the enablement requirement is satisfied.

Many of the techniques used to prepare the variants falling within the scope of the claims are described in the specification and include, e.g., recombinant and random mutagenesis techniques which are well known in the art. See the specification at page 7-9, 12-15, 25-29. Many preferred variants are also described in the specification, disclosing numerous alpha-amylases falling within the scope of the present invention. See the specification at page 16-25 and 32-37. The specification also provides general guidance how to select suitable positions to produce additional variants encompassed by the claims. See id.

The Examiner is also directed to Example 2-8 of the present specification in which a three dimensional model of SEQ ID NO:12 (AA560) was prepared (Example 3), information about important regions of the structure of SEQ ID NO:12 were obtained (Example 4), random mutagenesis was performed (Example 5), and numerous variants of SEQ ID NO:12 were constructed (Examples 6-8). The specification clearly exemplifies the exact skills an artisan can use to practice the invention commensurate in scope with the claims.

It is also respectfully submitted the claimed polypeptides are part of the very well studied Termamyl-like alpha-amylase family. The art provides significant guidance on the structure of this family of alpha-amylases, including guidance on suitable amino acid alterations, information as to which regions of the protein are involved particular functional activities, e.g., the active site resides, residues important for maintaining thermostability, and residues important for maintaining calcium stability. See, e.g., US Patent Nos. 6,528,298 and 6,297,039.

The Examiner again indicates that the claims can encompass $19^{485}$ variants as a basis for maintaining the rejection. However, the large number alone is not sufficient to show lack of enablement. "It is well established that a patent applicant is entitled to claim his invention generically when he describes it sufficiently to meet the [enablement requirement]." *Amgen* 927 F.2d at 1213. In this regard, requiring at least 90% homology with SEQ ID NO:12 makes the variants sufficiently similar in terms of structure and function so that the enablement requirement is satisfied.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

## II. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(b)

Claims 25, 27-28 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Outtrup et al. In summary, the Examiner alleges that although Outtrup et al. does not teach a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering), that the wild-type alpha-amylase of Outtrup et al. nevertheless reads on the claims because it has a lysine at one of the recited positions. The Examiner concludes that the claims therefore encompass the alpha-amylase of Outtrup et al. and therefore Outtrup et al. anticipates the claims. This rejection is respectfully traversed.

The alpha-amylase of Outtrup et al. does not read on the claims as the claims are directed to "variant" alpha-amylases having a "substitution" at an amino acid position 118, 320 and/or 458 (using SEQ ID NO:12 for numbering). As is well known in the art and described in the specification, a "variant" is a polypeptide in which alterations have been introduced into the amino acid sequence by man. See the specification at page 3 (under the heading "Nomenclature"). The claims are particularly directed to a "substitution" of a lysine at a position selected from the group consisting of 118, 320 and 458. As illustrated in the specification at page 3, a "substitution" is a change by man of one amino acid to another amino acid. Thus, the claims specifically exclude the wild-type enzyme of Outtrup et al. as Outtrup et al. does not disclose a variant having a substitution of a lysine at a position selected from the group consisting of 118, 320 and 458. Rather, the lysine is naturally present at the corresponding position in the alpha-amylase of Outtrup et al.

Thus, the claim are not anticipated because Outtrup et al. does not teach a variant alpha-amylase having a substitution at a position selected from the group consisting of 118, 320 and 458.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

## III. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(e)

Claims 25, 27-28 and 39 are rejected under 35 U.S.C. 102(e) as anticipated by US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031, and 6,887,986. The Examiner also alleges that although these patents do not teach a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering), that the wild-type alpha-amylases disclosed nevertheless read on the claims. This rejection is respectfully traversed.

The alpha-amylases of US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031 and 6,887,986 also do not read on the claims as they do not disclose variant alpha-amylases having a substitution of a lysine at a position selected from the group consisting of 118, 320 and 458. Each patent discloses the same wild-type parent amino acid. See the alignment provided by the Examiner. In this wild-type alpha-amylase, a substitution has not been made at position 118, 320 or 458. In this regard, the claims do not encompass the alpha-amylases recited in these patents as these patents do not claim or disclose a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering).

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

## IV. Double Patenting

Claims 25, 27-28 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Patent Nos. 6,093,526, 6,187,576, 6,197,565, 6,204,232, 6,297,038 and 6,673,589. This rejection is respectfully traversed.

The Examiner alleges that the claims are not patentably distinct from the claims of the instant application because all of the patents claim "a sequence that is 90% identical to SEQ ID NO:12 and comprise a change at position 320 and 458." It is respectfully submitted that the referenced patents does not disclose a change a position 320 and 458. Each patent discloses the same wild-type parent amino acid. See the alignment provided by the Examiner. In this wild-type alpha-amylase, a substitution has not been made at position 320 or 458. That is, the protein was isolated in nature having this amino acid sequence. Thus, these patents do not, as alleged by the Examiner, show a change or substitution at position 118, 320 or 458.

For the foregoing reasons, Applicants submit that the claims overcome the obviousness type double patenting rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

## V. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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